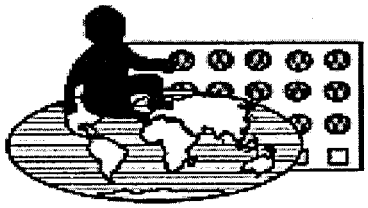

# Newborn Screening Quality Assurance Program

PROFICIENCY TESTING

Cystic Fibrosis Quarterly Report

Volume 4, No. 2

May 2005

## INTRODUCTION

The Cystic Fibrosis (CF) proficiency testing (PT) report is the quarterly summary of all data reported within the specified data-reporting period for Quarter 2, 2005. The attached tables provide the certification profiles (Immunoreactive Trypsinogen and DNA) for the distributed specimens, the verification of your reported data, the statistical analysis of the quantitative data, and the frequency distributions summary for presumptive clinical (qualitative) assessments. We distribute this PT report to all participants, state laboratory directors, and program colleagues by request.

On April 4, 2005, a panel of five unknown dried-blood-spot (DBS) specimens enriched with predetermined concentrations of IRT was distributed to 11 laboratories in the United States and 48 laboratories in other countries.

## PARTICIPANTS' RESULTS

We processed data from 49 participants. Laboratories were asked to report IRT results in ng/mL blood. For the statistical summary analysis, we did not include data that were outside the 99% confidence interval. There were eleven outliers for this survey. Results of our evaluation suggest that the endogenous level of IRT was less than 15 ng/mL blood.

Sixteen laboratories reported using Delfia to measure IRT, 23 used AutoDelfia, 2 used MP Biomedicals (ICN), 3 used BioRad Quantase, and the remaining 5 reported using "other." The expected IRT values are based on CDC assayed values. IRT is stable in the dried blood matrix. Table 1 illustrates comparability of the recovery of IRT from each specimen by method.

Presumptive clinical classifications (qualitative assessments) may differ by participant because of specific assessment practices. For participants that have provided us with their IRT cutoff value, we applied that cutoff in our final appraisal of the error judgment. Overall, participants reported one false-positive clinical assessment and no false-negative clinical assessments. Domestic and foreign laboratories reported various cutoffs for IRT. The median and mode cutoffs for domestic participants were 96.5 ng/mL blood and 90 ng/mL blood, respectively. The median and mode cutoffs for foreign participants were 72.4 ng/mL blood and 70 ng/mL blood, respectively.

We distributed DBS specimens containing DNA from Epstein-Barr virus-transformed lymphoblastoid cell lines homozygous for ΔF508 in a sheep whole blood matrix (specimens 2583 and 2585). These specimens were enriched with IRT to create proficiency testing materials that expressed both phenotype (elevated IRT) and genotype (ΔF508) for CF.

Participants were asked to confirm specimens that screened IRT positive. Sixteen laboratories reported DNA confirmatory results. Five laboratories reported using PCR amplification of DNA, 1 used Roche Linear Array, 1 used Innogenetics Auto-Lipa method, 2 used Innogenetics Inno-Lipa method, 1 used Tm Biosciences Tag-It Cystic Fibrosis kit, 3 used Oligonucleotide Ligation Assays, and 3 did not specify a method. There were no misclassifications of CF confirmed clinical assessments. One laboratory could not report data for specimen 2485 because of problems with amplification. One laboratory could not report data for both specimens 2483 and 2485 because of problems with amplification. We are continuing to evaluate our methods for preparing these specimens to avoid amplification failures by participants.❖

The Newborn Screening Quality Assurance Program will ship next quarter's Cystic Fibrosis PT specimens on July 11, 2005.❖

CDC/APHL

This program is cosponsored by the Centers for Disease Control and Prevention (CDC) and the Association of Public Health Laboratories (APHL).

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NEWBORN SCREENING QUALITY ASSURANCE PROGRAM

*CYSTIC FIBROSIS - IRT*

QUARTER II - MAY 2005

LAB

## SPECIMEN CERTIFICATION - IRT

CDC ASSAYED LEVELS

| Analyte | Specimen 2581 | Specimen 2582 | Specimen 2583 | Specimen 2584 | Specimen 2585 |
|---|---|---|---|---|---|
| Immunoreactive Trypsinogen CDC Mean Assayed Value (ng/mL blood) | 20.1 ± 3.1 | 36.2 ± 2.8 | 304.2 ± 44.2 | 11.3 ± 1.8 | 180.2 ± 14.1 |

EXPECTED PRESUMPTIVE CLINICAL ASSESSMENTS

| Disorder | Specimen 2581 | Specimen 2582 | Specimen 2583 | Specimen 2584 | Specimen 2585 |
|---|---|---|---|---|---|
| Cystic Fibrosis | 1 | 1 | 2 | 1 | 2 |

01 = within normal limits 02 = outside normal limits NE = clinical assessment not evaluated

## DATA VERIFICATION

| Analyte | Specimen 2581 | | Specimen 2582 | | Specimen 2583 | | Specimen 2584 | | Specimen 2585 | |
|---|---|---|---|---|---|---|---|---|---|---|
| | Result | Code | Result | Code | Result | Code | Result | Code | Result | Code |
| Immunoreactive Trypsinogen (ng/mL blood) | | | | | | | | | | |

01 = within normal limits 02 = outside normal limits NE = clinical assessment not evaluated

*Reviewer's Comments*

EVALUATION:

NEWBORN SCREENING QUALITY ASSURANCE PROGRAM

*CYSTIC FIBROSIS - IRT*

QUARTER II - MAY 2005

## OVERALL STATISTICS - IRT

| Specimen | N* | Outliers | Mean | UL (95%) | LL (95%) |
|---|---|---|---|---|---|
| 2581 | 48 | 1 | 19.7 | 28.3 | 11.1 |
| 2582 | 46 | 3 | 38.1 | 49.3 | 27 |
| 2583 | 47 | 2 | 282.5 | 412.2 | 152.8 |
| 2584 | 45 | 4 | 11.4 | 15.8 | 6.9 |
| 2585 | 46 | 3 | 172.1 | 251.1 | 93.2 |

* Outliers are not included in N. UL = upper limit LL = lower limit

## FREQUENCY DISTRIBUTION OF PARTICIPANTS' CLINICAL ASSESSMENTS

| Specimen | Within Normal Limits | Outside Normal Limits |
|---|---|---|
| 2581 | 48 | 1 |
| 2582 | 49 | 0 |
| 2583 | 0 | 49 |
| 2584 | 49 | 0 |
| 2585 | 0 | 49 |

NEWBORN SCREENING QUALITY ASSURANCE PROGRAM

*CYSTIC FIBROSIS - DNA*

QUARTER II - MAY 2005

LAB

SPECIMEN CERTIFICATION - DNA

CDC IDENTIFIED GENOTYPES

| Analyte | Specimen 2581 | Specimen 2582 | Specimen 2583 | Specimen 2584 | Specimen 2585 |
|---|---|---|---|---|---|
| DNA | Wild Type (Normal) | Wild Type (Normal) | ΔF508/ΔF508 | Wild Type (Normal) | ΔF508/ΔF508 |

EXPECTED DNA CONFIRMED CLINICAL ASSESSMENTS

| Disorder | Specimen 2581 | Specimen 2582 | Specimen 2583 | Specimen 2584 | Specimen 2585 |
|---|---|---|---|---|---|
| Cystic Fibrosis | 1, 4 | 1, 4 | 2 | 1, 4 | 2 |

1 = wild type (normal) 2 = cystic fibrosis positive 3 = cystic fibrosis carrier 4 = not tested

DATA VERIFICATION

| Analyte | Specimen 2581 | | Specimen 2582 | | Specimen 2583 | | Specimen 2584 | | Specimen 2585 | |
|---|---|---|---|---|---|---|---|---|---|---|
| | Result | Code | Result | Code | Result | Code | Result | Code | Result | Code |
| DNA | | | | | | | | | | |

1 = wild type (normal) 2 = cystic fibrosis positive 3 = cystic fibrosis carrier 4 = not tested

*Reviewer's Comments*

EVALUATION:

NEWBORN SCREENING QUALITY ASSURANCE PROGRAM

*CYSTIC FIBROSIS - DNA*

QUARTER II - MAY 2005

## SUMMARY OF PARTICIPANTS' GENOTYPES

| Specimen | Genotype | N |
|---|---|---|
| 2581 | Wild Type/Wild Type | 4 |
| 2582 | Wild Type/Wild Type | 4 |
| 2583 | ΔF508/ΔF508 | 16 |
| 2584 | Wild Type/Wild Type | 4 |
| 2585 | ΔF508/ΔF508 | 15 |

## FREQUENCY DISTRIBUTION OF PARTICIPANTS' CLINICAL ASSESSMENTS

| Specimen | Wild Type (Normal) | Cystic Fibrosis Positive | Cystic Fibrosis Carrier | Not Tested |
|---|---|---|---|---|
| 2581 | 4 | 0 | 0 | 13 |
| 2582 | 4 | 0 | 0 | 13 |
| 2583 | 0 | 16 | 0 | 0 |
| 2584 | 4 | 0 | 0 | 13 |
| 2585 | 0 | 15 | 0 | 0 |

NEWBORN SCREENING QUALITY ASSURANCE PROGRAM

*CYSTIC FIBROSIS - IRT*

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## IMMUNOREACTIVE TRYPSINOGEN BY METHOD

Table 1. Recovery of IRT (ng/mL blood) by method

| Specimen No. | Specimen 2581 | Specimen 2582 | Specimen 2583 | Specimen 2584 | Specimen 2585 |
|---|---|---|---|---|---|
| Expected Value | 20.1 | 36.2 | 304.2 | 11.3 | 180.2 |
| Method (N) | | | | | |
| Delfia (16) | 20.8 ± 3.0 | 37.1 ± 6.4 | 286.4 ± 42.9 | 12.3 ± 4.8 | 178.8 ± 28.8 |
| AutoDelfia (23) | 19.6 ± 3.3 | 40.5 ± 5.4 | 305.0 ± 33.9 | 11.5 ± 1.4 | 185.4 ± 27.8 |
| MP (ICN) (2) | 26.9 ± 5.5 | 38.9 ± 2.5 | 343.8 ± 149.6 | 18.5 ± 1.1 | 276.0 ± 79.9 |
| Bio-Rad (3) | 12.5 ± 2.7 | 31.2 ± 3.6 | 221.0 ± 73.3 | 10.8 ± 3.2 | 113.2 ± 41.3 |
| Other (5) | 18.1 ± 6.9 | 33.5 ± 12.2 | 106.0 ± 48.1 | 7.5 ± 0.7 | 71.0 ± 45.3 |

N = Number of observations